

Challenging Issues in Clinical Research

HS

In this issue of the ACRP *Monitor*, three articles have been selected as the basis for a Home Study test that contains 30 questions. For your convenience, the articles and questions are provided in print as well as online (members only) in the form of a PDF (requires Adobe Reader and text file). This activity is anticipated to take three hours.

Answers must be submitted using the electronic answer form online (members only, \$32). Those who answer 70% of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

Hardware/Software Requirements: Home Study tests require version 4.x browsers or higher from Internet Explorer, Mozilla Firefox, or Safari. A browser that can run Adobe Flash 9.0 is required to view the digital edition of *The Monitor*, and Adobe Acrobat is required to view PDFs of the Home Study test.

The **August 2011 *Monitor* Home Study** is based on the following three articles in this issue:

- 1. International Ethics and Social Responsibility**
 Frank Wells, MBBS, FRCP, FRCPE, FPPM, U.K. National Research Ethics Advisor
- 2. How Can Sponsors and Health Authorities Cope With the Drive for More Inspections?**
 Kristel Van de Voorde, MPharm, Director, Global Quality Regulatory Compliance Division at Bristol-Myers Squibb
- 3. Demystifying Fair Market Value**
 Beth D. Harper, MBA, Chief Clinical Officer, Centerphase Solutions, Inc. | Kevin T. Williams, MBA, MS, Vice President and General Manager for Global Contract Management Services, Clinical Financial Services

HOME STUDY LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

- understand the structure, function, and history of research ethics committees worldwide, while also examining research integrity in general.
- understand the reasons and consequences of the increased number of inspections related to clinical trials.
- describe the concept of fair market value.

This test expires on AUGUST 31, 2012

(original release date: 08/01/2011)

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QUESTIONS 1–10

International Ethics and Social Responsibility

1 In 1948 the Nuremberg Code was established. In what year was the Declaration of Helsinki established?

- A. 1963
- B. 1964
- C. 1965
- D. 1969

2 What are the ethical principles for human research?

- A. Interest in status and financial gain
- B. Acceptance of statistical results
- C. Beneficence, justice, and respect for persons
- D. Respect for research colleagues

3 Definitions and guidance for research ethics committees are contained in which of the following regulations?

- 1. Nuremberg Code
- 2. ICH-GCP
- 3. Volume 9A
- 4. EC GCP Directive

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

4 EFGCP key strategy is to promote the values and principles in research ethics in the international region, which led to what report being published in 2007 and updated in 2010?

- A. EFGCP Ethics Report
- B. EFGCP Belmont Report
- C. EFGCP Ethics Committees Report
- D. EFGCP Report

5 What are the advantages of having a regulated REC environment?

- 1. Uniform performance
- 2. Consistent conclusions and opinions
- 3. No continuity in performance of RECs
- 4. General approach adopted by all RECs

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

6 Which of the following are examples of training conducted by RECs worldwide?

- 1. Course in pharmacovigilance activities
- 2. Programs for new members
- 3. Ethics course for members of local RECs
- 4. Training program for REC members

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

7 What are the key differences between IRBs in Europe and those in the U.S.?

- 1. In U.S. are managed as institutions
- 2. In Europe and U.S. conducted as independent boards
- 3. In Europe are managed as independent bodies
- 4. In Europe and U.S. conducted as a business

- A. 1 and 3 only
- B. 1 and 4 only
- C. 2 and 3 only
- D. 2 and 4 only

8 What are some considerations when creating RECs in the U.K.?

- 1. Geographic location
- 2. Lay members can work for local research institutions
- 3. Lay members not allowed to work for any research institutions near REC district
- 4. REC must be independent

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

9 Which of the following are examples of misconduct in medical research?

- 1. Immunologist faked a skin transplant
- 2. University professor fabricated data
- 3. Oncologist used fake data in a publication
- 4. Pediatrician inadvertently recorded wrong data in a CRF

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

10 Which of the following describes issues addressed in the “Singapore Statement”?

- 1. Development of guidelines
- 2. Honesty and accountability
- 3. Integrity, adherence to regulations, and codes of conduct
- 4. Research environments and community considerations

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

QUESTIONS 11–20

How Can Sponsors and Health Authorities Cope With the Drive for More Inspections?

11 The increase in the number of inspections by the EMA is driven by the increase in:

- A. the number of trials.
- B. the amount of patients in trials.
- C. personnel for inspection resources.
- D. trials with a majority of patients from outside Europe.

12 How many Marketing Authorization Applications does EMA inspect?

- A. About 1%
- B. About 10%
- C. About 50%
- D. 100%

13 Which health authorities have started capacity building for inspections by participating in trainings by the U.S. FDA?

- A. India, China, and Hong Kong
- B. China, Hong Kong, and Taiwan
- C. India and China
- D. India, Korea, and Singapore

14 When do sponsor subject matter experts on computer validation need to be available for an inspection?

- 1. Before a sponsor inspection occurs
- 2. During a site inspection
- 3. Prior to submission of the Marketing Authorization
- 4. As soon as a sponsor inspection occurs

- A. 1, 2, and 3 only
- B. 1, 2, and 4 only
- C. 1, 3, and 4 only
- D. 2, 3, and 4 only

CORRECTIONS

Corrections to Home Studies can be found on the ACRP website and are incorporated directly into the online test.

15 What is the scope of a site inspection?

1. Conduct of the study by investigator
 2. Oversight by the sponsor
 3. Validation of electronic medical record system at the hospital
 4. Reimbursement practices at the hospital
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

16 Companies cope with the increase in inspections by:

- A. refusing inspections due to lack of personnel or infrastructure.
- B. writing more procedures to increase efficiency around inspections.
- C. not attending inspections in person, and receiving results after the inspection.
- D. setting up internal inspection management groups.

17 How are health authorities changing their approach to select sites for inspection?

- A. Making risk assessments based on information collected on compliance status and risk control
- B. Selecting the highest recruiting sites within each geographic region of the study
- C. Choosing sites at random using a scientifically valid statistical tool
- D. Deferring to the advice of the scientific advisor within their compliance department

18 What is the aim of FDA's risk-based prioritization tool piloted in 2010?

1. Inspect ongoing studies
 2. Conduct more inspections
 3. Allow action plan implementation to minimize risk to subjects
 4. Preserve integrity of the trials
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

19 Health authorities like EMA and FDA try to eliminate duplication of work by:

- A. conducting inspections in their geographic region only.
- B. sharing inspection information and conducting joint inspections.
- C. inspecting sites not previously audited by a sponsor.
- D. relying on inspection reports by other country health authorities.

20 An application to EMA needs to include the following in order to determine the need for additional inspections:

- A. List of monitoring visit details
- B. Issues and actions logs maintained during the project management
- C. List of audits and regulatory inspections of which the applicant is aware
- D. List of protocol deviations and serious adverse events

QUESTIONS 21–30 Demystifying Fair Market Value

21 Confusion regarding FMV results in which of the following outcomes?

1. Protracted budget negotiations
 2. Failure to negotiate a successful budget agreement
 3. Delayed study startup timelines
 4. A higher likelihood of a sponsor or site being audited
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

22 The origins of the concept of FMV in the United States date back to a report from the Office of Inspector General (OIG) written in:

- A. 2000
- B. 2003
- C. 2005
- D. 2007

23 Which of the following statements best describes how FMV is defined?

- A. The Food and Drug Administration has finalized the definition.
- B. The description found in the dictionary is the most accurate.
- C. The Office of Inspector General (OIG) has determined it.
- D. There is no unified or official definition of FMV.

24 Federal and state regulations and _____ are among the primary factors affecting FMV practices.

- A. Investigator experience
- B. Sponsor standard operating procedures
- C. Professional codes of conduct
- D. Prosecutor and regulatory inspector biases

25 The key concern related to FMV principles is the potential for payment to investigators to influence which of the following?

- A. The safety profile of the investigational product
- B. Faster clinical trial enrollment
- C. Prescribing behavior or medical decision-making
- D. Reduced dropout rates

26 Although different methods might be used to calculate the payment to an investigator, which of the following determines whether the payment amount itself is “fair”?

- A. The Office of Inspector General (OIG) guidelines
- B. Thresholds defined by the federal regulations
- C. Historical data
- D. The reasonableness of the payment in relationship to the work effort

27 In addition to procedure costs, regional differences, and historical payments, “fair” payment determination should also consider:

- A. personnel costs associated with conducting the trial.
- B. investigator experience.
- C. quality of the investigator's work.
- D. key opinion leader status of the investigator.

28 To ensure compliance with FMV principles, sponsor payment determination and practices should:

1. be consistent across investigators.
 2. be transparent.
 3. rely heavily on internal historical fee data.
 4. be defensible.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

29 Compliance with FMV principles requires that sponsor payments to investigators for the same level of service:

- A. be identical for each investigator.
- B. be fair and consistent across sites.
- C. not vary by more than +/-10%.
- D. be publicly disclosed on an annual basis.

30 To aid in FMV compliance, investigative sites should:

1. subscribe to benchmarking databases.
 2. justify and document their work effort.
 3. assess their true costs of performing services.
 4. assure transparency in their compensation to investigators.
- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only